



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>A61K 31/57 // (A61K 31/57, 31:565)</b>		A3	(11) International Publication Number: <b>WO 97/48367</b> (43) International Publication Date: 24 December 1997 (24.12.97)
<p>(21) International Application Number: <b>PCT/GB97/01653</b></p> <p>(22) International Filing Date: 18 June 1997 (18.06.97)</p> <p>(30) Priority Data: 9612990.3 20 June 1996 (20.06.96) GB</p> <p>(71) Applicant (for all designated States except US): STANFORD ROOK LIMITED [GB/GB]; Glen House, 200-208 Tottenham Court Road, London W1P 9LA (GB).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): ROOK, Graham, Arthur, William [GB/GB]; Stanford Rook Limited, Glen House, 200-208 Tottenham Court Road, London W1P 9LA (GB). PANDO HERNANDEZ, Rogelio [MX/MX]; Instituto Nacional de la Nutrición Salvador Zubirán, Dept. Pathology, Calle Vasco de Quiroga 15, Delegación Tlalpan, Mexico, D.F. 14000 (MX).</p> <p>(74) Agents: WALTON, Sean, M. et al.; Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP (GB).</p>		<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments. In English translation (filed in Finnish).</i></p> <p>(88) Date of publication of the international search report: 5 February 1998 (05.02.98)</p>	
<p>(54) Title: COMPOSITIONS FOR THE TREATMENT OF CHRONIC INFECTIONS CONTAINING GLUCOCORTICOID AND ANTI-GLUCOCORTICOID</p> <p>(57) Abstract</p> <p>A glucocorticoid, such as cortisol or a derivative or analogue thereof, and an anti-glucocorticoid, such as dehydroepiandrosterone (DHEA) or a derivative or analogue thereof, are used simultaneously, separately or sequentially in treatment of chronic infections such as tuberculosis, HIV infection, leishmaniasis and syphilis.</p>			

***FOR THE PURPOSES OF INFORMATION ONLY***

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

# INTERNATIONAL SEARCH REPORT

Int. Application No  
PCT/GB 97/01653

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 6 A61K31/57 // (A61K31/57, 31:565)

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 387 583 A (LORIA ROGER M) 7 February 1995 see abstract see page 4, line 20-29 see page 5, line 45-68; examples 1-6 ---	1-19
X	WO 91 04030 A (UNIV UTAH) 4 April 1991 see page 13, line 25 - page 14, line 5; figures 2A,2B,2C; example 2 see claim 4; example 4 ---	1-5,8-12
P,X	US 5 540 919 A (DAYNES RAYMOND A ET AL) 30 July 1996 see page 5, line 51-64; claims 9-12; figures 2A,2B,2C,4 ---	1-5, 8-12, 14-18 -/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

2

Date of the actual completion of the international search

31 October 1997

Date of mailing of the international search report

16.12.97

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl  
Fax: (+31-70) 340-3016

Authorized officer

Gonzalez Ramon, N

## INTERNATIONAL SEARCH REPORT

In	ntional Application No
PCT/GB 97/01653	

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 077 284 A (LORIA ROGER M ET AL) 31 December 1991 see abstract see page 11, line 35-45 see page 13, line 55-68; claims 1-3 ---	1-19
A	WISNIEWSKI TL ET AL: "The relationship of serum DHEA-S and cortisol levels to measures of immune function in human immunodeficiency virus-related illness." AM J MED SCI, FEB 1993, 305 (2) P79-83, UNITED STATES, XP002044510 see page 80, column 1, paragraph 1; figure 3 ---	1,2,4-6, 8,9, 11-15
A	BAKER R.W. ET AL: "Tuberculosis, steroid metabolism and immunity" QJM - MONTHLY JOURNAL OF THE ASSOCIATION OF PHYSICIANS, 1996, 89/5 (387-394), UNITED KINGDOM, XP002044502 see page 388, column 2, paragraph 2 - page 389, column 1, paragraph 2 see page 390, column 2, paragraph 4 ---	1,2,4-6, 8,9, 11-15
A	ROOK G A W ET AL: "Pathogenetic role, in human and murine tuberculosis, of changes in the peripheral metabolism of glucocorticoids and antiglucocorticoids" PSYCHONEUROENDOCRINOLOGY, 22 (SUPPL. 1). 1997. S109-S113., XP002044516 see page 112, paragraph 3 ---	1-19
A	DE 38 12 595 A (COLTHURST LTD ;PRENDERGAST PATRICK THOMAS (IE)) 27 October 1988 see abstract; claims 3-6; examples 8,9 ---	1-19
A	WO 95 30418 A (UNIV JOHNS HOPKINS) 16 November 1995 see abstract see page 3, line 19-30; claims 1,9,11,13 -----	1-19

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 97/01653

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

Claims Nos.: 1-13

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

In view of the large number of compounds, which are defined by the general definition in the independent claims, the search had to be restricted for economic reasons. The search was limited to the compounds for which pharmacological data was given and/or the compounds mentioned in the claims, and to the general idea underlying the application (see Guidelines, Part B, Chapter III, paragraph 3.6).

Remark : Although claims 14-19 are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the compound/composition.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No	PCT/GB 97/01653
---------------------	-----------------

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5387583 A	07-02-95	WO 9423722 A	27-10-94
-----			
WO 9104030 A	04-04-91	AU 652130 B AU 6501990 A AU 667018 B AU 7572794 A CA 2066716 A EP 0494224 A JP 2505313 B JP 5502856 T US 5540919 A US 5562910 A US 5518725 A	18-08-94 18-04-91 29-02-96 08-12-94 26-03-91 15-07-92 05-06-96 20-05-93 30-07-96 08-10-96 21-05-96
-----			
US 5540919 A	30-07-96	AU 652130 B AU 6501990 A AU 667018 B AU 7572794 A CA 2066716 A EP 0494224 A JP 2505313 B JP 5502856 T WO 9104030 A US 5562910 A US 5518725 A	18-08-94 18-04-91 29-02-96 08-12-94 26-03-91 15-07-92 05-06-96 20-05-93 04-04-91 08-10-96 21-05-96
-----			
US 5077284 A	31-12-91	US 5461042 A US 5407684 A	24-10-95 18-04-95
-----			
DE 3812595 A	27-10-88	AT 401470 B AT 98488 A AU 608824 B AU 1467888 A BE 1004315 A CA 1325594 A CH 675358 A DK 208188 A FR 2615394 A GB 2204237 A,B GR 88100248 A	25-09-96 15-02-96 18-04-91 20-10-88 03-11-92 28-12-93 28-09-90 17-10-88 25-11-88 09-11-88 31-01-89

# INTERNATIONAL SEARCH REPORT

Information on patent family members

In	International Application No
	PCT/GB 97/01653

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 3812595 A		JP 1025722 A JP 2577771 B KR 9614988 B LU 87202 A NL 8800926 A NZ 236303 A OA 8729 A PH 25907 A SE 503482 C SE 8801406 A US 4956355 A	27-01-89 05-02-97 23-10-96 17-11-88 16-11-88 27-07-97 31-03-89 19-12-91 24-06-96 17-10-88 11-09-90
WO 9530418 A	16-11-95	AU 2473695 A	29-11-95